

CLAIMS

1. A method of treating a neurological condition in a mammal, comprising administering
to the mammal a hematopoietic factor selected from the group consisting of GMCSF,
a GMCSF derivative, GCSF, a GCSF derivative, and combinations thereof in an
5 amount sufficient to treat the neurological condition.
2. The method of Claim 1, wherein said neurological condition is selected from the
group consisting of a neurological disease with pathophysiological mechanisms
involving ischemia, a neurological disease with pathophysiological mechanisms
involving hypoxia, a neurodegenerative disease, and a disease of the nervous system
10 accompanied by neural cell death.
3. The method of Claim 1, wherein the neurological condition is neurological disease
with pathophysiological mechanisms involving ischemia or hypoxia.
4. The method of Claim 3, wherein the neurological disease with pathophysiological
mechanisms involving ischemia or hypoxia is stroke.
- 15 5. The method of Claim 1, further comprising administering one or more additional
hematopoietic factors.
6. The method of Claim 5, wherein the additional hematopoietic factors are selected
from the group consisting of a macrophage stimulating factor, an interleukin, and
erythropoietin.
- 20 7. The method of Claim 6, wherein GCSF and erythropoietin are administered to the
mammal.
8. The method of Claim 1, wherein the neurological condition is stroke, Parkinson's
disease, amyotrophic lateral sclerosis, neurotrauma, cerebral ischemia due to cardiac
arrest, or cerebral ischemia during an operative procedure..

9. The method of Claim 1, wherein the hematopoietic factor is GCSF or a GCSF derivative.
10. The method of Claim 1, wherein the hematopoietic factor is GMCSF or a GMCSF derivative.
- 5 11. The method of Claim 1, which further comprises administering a hemodynamically active compound.
12. The method of Claim 1, which further comprises administering tissue plasminogen activator to the mammal.
- 10 13. The method of Claim 1, which further comprises administering an agent that facilitates passage over the blood brain barrier.
14. The method of Claim 1, which further comprises administering an anti-apoptotic agent.
15. The method of Claim 12, wherein the neurological condition is stroke.
16. The method of Claim 7, further comprising administering tissue plasminogen activator to the mammal.
- 15 17. The method of Claim 1, wherein the hematopoietic factor is a human factor or derived from a human factor.
18. The method of Claim 1, wherein the mammal is human.
19. The method of Claim 1, wherein the hematopoietic factor is administered by one or
- 20 more modes of administration selected from the group consisting of direct intracerebral injection, intravenously, intraarterially, orally, and subcutaneously.
20. The method of Claim 1, wherein the administering the hematopoietic factor comprises administering a polynucleotide, which when administered in the mammal expresses the hematopoietic factor in an amount sufficient to treat the neurological condition.

21. The method of Claim 20, wherein the polynucleotide is administered with a viral vector or a liposome.

22. A method of treating a neurological condition in a mammal, comprising contacting a neural stem cell composition with a hematopoietic factor selected from the group consisting of GMCSF, a GMCSF derivative, GCSF, a GCSF derivative, and combinations thereof; and subsequently administering the neural stem cells to a mammal in need thereof.

23. The method of Claim 22, wherein said neurological condition is selected from the group consisting of a neurological disease with pathophysiological mechanisms involving ischemia, a neurological disease with pathophysiological mechanisms involving hypoxia, a neurodegenerative disease, and a disease of the nervous system accompanied by neural cell death.

24. The method of Claim 23, a neurological disease with pathophysiological mechanisms involving ischemia or hypoxia.

25. The method of Claim 24 wherein the neurological disease with pathophysiological mechanisms involving ischemia or hypoxia is stroke.

26. The method of Claim 22, further comprising contacting the neural stem cell composition with one or more additional hematopoietic factors.

27. The method of Claim 26, wherein the additional hematopoietic factors are selected from the group consisting of a macrophage stimulating factor, an interleukin, and erythropoietin.

28. The method of Claim 27, wherein the neural stem cell composition is contacted with GCSF and erythropoietin.

29. The method of Claim 22, wherein the neurological condition is stroke, Parkinson's disease, amyotrophic lateral sclerosis, neurotrauma, cerebral ischemia due to cardiac arrest, or cerebral ischemia during an operative procedure.

30. The method of Claim 22, wherein the hematopoietic factor is GCSF or a GCSF derivative.

31. The method of Claim 22, wherein the hematopoietic factor is GMCSF or a GMCSF derivative.

32. The method of Claim 22, wherein the hematopoietic factor is a human factor or derived from a human factor.

33. The method of Claim 22, wherein the mammal is human.

34. The method of Claim 22, wherein the neural stem cell composition comprises human neural stem cells.

35. A method for identifying a compound that binds to the granulocyte colony stimulating factor receptor on neuronal cells and which activates STAT in the neuronal cell, comprising contacting the neuronal cell with the compound; and measuring an increase in STAT activation relative to STAT activation in a neuronal cell which has not been contacted with the compound, wherein an increase in STAT activation is indicative of a compound that binds to the granulocyte colony stimulating factor receptor on the neuronal cell.

36. The method of Claim 35, wherein the STAT gene is STAT-3.

37. The method of Claim 35, wherein the STAT gene is STAT-5.

38. A compound identified according to the method of Claim 35.

39. A method of treating a neurological condition in a mammal, comprising administering to the mammal the compound of Claim 38 in an amount sufficient to treat the neurological condition.

40. The method of Claim 39, wherein said neurological condition is selected from the group consisting of a neurological disease with pathophysiological mechanisms involving ischemia, a neurological disease with pathophysiological mechanisms involving hypoxia, a neurodegenerative disease, and a disease of the nervous system accompanied by neural cell death.
41. The method of Claim 40, wherein said neurological condition is a neurological disease with pathophysiological mechanisms involving ischemia.
42. The method of Claim 41, wherein the neurological disease with pathophysiological mechanisms involving ischemia or hypoxia is stroke.
43. The method of Claim 42, which further comprises administering tissue plasminogen activator to the mammal.
44. The method of Claim 39, further comprising administering one or more additional hematopoietic factors.
45. The method of Claim 44, wherein the additional hematopoietic factors are selected from the group consisting of a macrophage stimulating factor, an interleukin, and erythropoietin.
46. The method of Claim 39, which further comprises administering a hemodynamically active compound.
47. The method of Claim 39, which further comprises administering an agent that facilitates passage over the blood brain barrier.
48. The method of Claim 39, which further comprises administering an antiapoptotic agent
49. The method of Claim 39, wherein the mammal is human.

50. The method of Claim 39, wherein the compound is administered by one or more modes of administration selected from the group consisting of direct intracerebral injection, intravenously, intraarterially, orally, and subcutaneously.

51. The method of Claim 39, wherein the neurological condition is stroke, Parkinson's disease, amyotrophic lateral sclerosis, neurotrauma, cerebral ischemia due to cardiac arrest, or cerebral ischemia during an operative procedure.

52. A method for identifying a compound that binds to the granulocyte macrophage colony stimulating factor receptor on neuronal cells and/or which activates STAT gene expression in the neuronal cell, comprising contacting the neuronal cell with the compound; and measuring an increase in STAT activation relative to STAT gene activation in a neuronal cell which has not been contacted with the compound, wherein an increase in STAT activation is indicative of a compound that binds to the granulocyte macrophage colony stimulating factor receptor on the neuronal cell.

53. The method of Claim 52, wherein the STAT gene is STAT-3.

54. The method of Claim 52, wherein the STAT gene is STAT-5.

55. A compound identified according to the method of Claim 52.

56. A method of treating a neurological condition in a mammal, comprising administering to the mammal the compound of Claim 55 in an amount sufficient to treat the neurological condition.

57. The method of Claim 56, wherein said neurological condition is selected from the group consisting of a neurological disease with pathophysiological mechanisms involving ischemia, a neurological disease with pathophysiological mechanisms involving hypoxia, a neurodegenerative disease, and a disease of the nervous system accompanied by neural cell death..

58. The method of Claim 57, wherein the neurological condition is a neurological disease with pathophysiological mechanisms involving ischemia or hypoxia.

59. The method of Claim 58, wherein the neurological disease with pathophysiological mechanisms involving ischemia is stroke.

5 60. The method of Claim 59, which further comprises administering tissue plasminogen activator to the mammal.

61. The method of Claim 56, further comprising administering one or more additional hematopoietic factors.

10 62. The method of Claim 61, wherein the additional hematopoietic factors are selected from the group consisting of a macrophage stimulating factor, an interleukin, and erythropoietin.

63. The method of Claim 56, wherein the mammal is human.

15 64. The method of Claim 56, wherein the compound is administered by one or more modes of administration selected from the group consisting of direct intracerebral injection, intravenously, intraarterially, orally, and subcutaneously.

20 65. A method for identifying a compound with improved GCSF receptor agonist activity, comprising contacting the compound with a neural cell having a GCSF receptor, measuring the neuroprotective effect of the compound to the neural cell, and comparing the effect of the compound to the effect of GCSF, wherein a higher neuroprotective effect with the compound relative to the effect of GCSF indicates that the compound has improved GCSF receptor agonist activity.

66. A compound identified according to the method of Claim 64.

25 67. A method of treating a neurological condition in a mammal, comprising administering to the mammal the compound of Claim 65 in an amount sufficient to treat the neurological condition.

68. The method of Claim 66, wherein said neurological condition is selected from the group consisting of a neurological disease with pathophysiological mechanisms involving ischemia, a neurological disease with pathophysiological mechanisms involving hypoxia, a neurodegenerative disease, and a disease of the nervous system accompanied by neural cell death..
69. The method of Claim 67, wherein the neurological condition is a neurological disease with pathophysiological mechanisms involving ischemia.
70. The method of Claim 68, wherein the neurological disease with pathophysiological mechanisms involving ischemia is stroke.
71. The method of Claim 69, which further comprises administering tissue plasminogen activator to the mammal.
72. The method of Claim 66, further comprising administering one or more additional hematopoietic factors.
73. The method of Claim 71, wherein the additional hematopoietic factors are selected from the group consisting of a macrophage stimulating factor, an interleukin, and erythropoietin.
74. The method of Claim 66, wherein the mammal is human.
75. The method of Claim 66, wherein the compound is administered by one or more modes of administration selected from the group consisting of direct intracerebral injection, intravenously, intraarterially, orally, and subcutaneously.
76. The method of Claim 66, wherein the neurological condition is stroke, Parkinson's disease, amyotrophic lateral sclerosis, neurotrauma, cerebral ischemia due to cardiac arrest , or cerebral ischemia during an operative procedure.
77. A method for identifying a compound with improved GCSF receptor agonist activity, comprising contacting the compound with a neural cell having a GCSF receptor,

comparing the level of STAT gene expression in the neural cell to a second neural cell contacted with GCSF, wherein an increase in STAT activation in the neural cell contacted with the compound relative to the STAT activation in the second neural cell indicates that the compound has improved GCSF receptor agonist activity.

5 78. The method of Claim 77, wherein the STAT activation is one or both of STAT3 and STAT5 activation.

79. A compound identified according to the method of Claim 77.

80. A method of treating a neurological condition in a mammal, comprising administering to the mammal the compound of Claim 79 in an amount sufficient to treat the
10 neurological condition.

81. The method of Claim 80, wherein said neurological condition is selected from the group consisting of a neurological disease with pathophysiological mechanisms involving ischemia, a neurological disease with pathophysiological mechanisms involving hypoxia, a neurodegenerative disease, and a disease of the nervous system
15 accompanied by neural cell death..

82. The method of Claim 80, wherein the neurological condition is a neurological disease with pathophysiological mechanisms involving ischemia or hypoxia.

83. The method of Claim 81, wherein the neurological disease with pathophysiological mechanisms involving ischemia or hypoxia is stroke.

20 84. The method of Claim 80, which further comprises administering tissue plasminogen activator to the mammal.

85. The method of Claim 80, further comprising administering one or more additional hematopoietic factors.

86. The method of Claim 85, wherein the additional hematopoietic factors are selected from the group consisting of a macrophage stimulating factor, an interleukin, and erythropoietin.

87. The method of Claim 80, wherein the mammal is human.

5 88. The method of Claim 80, wherein the compound is administered by one or more modes of administration selected from the group consisting of direct intracerebral injection, intravenously, intraarterially, orally, and subcutaneously.

89. The method of Claim 80, wherein the neurological condition is stroke, Parkinson's disease, amyotrophic lateral sclerosis, neurotrauma, cerebral ischemia due to cardiac arrest , or cerebral ischemia during an operative procedure.

10 90. A method of enhancing the survival of a cell transplanted into a mammal, comprising introducing into the cell one or more polynucleotides which encode a hematopoietic factor selected from the group consisting of GMCSF, a GMCSF derivative, GCSF, a GCSF derivative, and combinations thereof, wherein the cell expresses the
15 hematopoietic factor in an amount sufficient to enhance the survival of the cell relative to the cell survival prior to introducing the one or more polynucleotides.

91. The method of Claim 90, wherein the cell further expresses and secretes one or more additional hematopoietic factors.

20 92. The method of Claim 94, wherein the additional hematopoietic factors are selected from the group consisting of a macrophage stimulating factor, an interleukin, and erythropoietin.

93. The method of Claim 90, wherein the hematopoietic factor is GCSF or a GCSF derivative.

25 94. The method of Claim 90, wherein the hematopoietic factor is GMCSF or a GMCSF derivative.

95. The method of Claim 90, wherein the mammal is human.

96. The method of Claim 90, wherein the cell is a neural cell.

97. The method of Claim 96, wherein the neural cell is a neural stem cell.

98. The method of Claim 90, wherein the cell is a stem cell.

5 99. The method of Claim 90, wherein the cell further expresses one or both of a GCSF receptor and a GMCSF receptor.

100. The method of Claim 90, wherein the cell is transplanted into neural tissue of the mammal.

101. A method of enhancing the viability of a neural cell culture comprising
10 contacting the neural cell culture with a hematopoietic factor selected from the group consisting of GMCSF, a GMCSF derivative, GCSF, a GCSF derivative, and combinations thereof in an amount sufficient to enhance the viability of the neural cell culture relative to the culture prior to contacting with the hematopoietic factor.

102. The method of Claim 101, wherein the neural cell culture comprises neural
15 stem cells.

103. A method of enhancing the viability of a neural cell culture comprising
introducing one or more polynucleotides into the cells of the neural cell culture wherein the polynucleotide expresses a hematopoietic factor selected from the group consisting of GMCSF, a GMCSF derivative, GCSF, a GCSF derivative, and
20 combinations thereof, and wherein the polynucleotide expresses the hematopoietic factor in an amount sufficient to enhance the viability of the neural cell culture relative to the culture prior to contacting with the hematopoietic factor.

104. The method of Claim 103, wherein the polynucleotide is administered with a viral vector or a liposome

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